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Harde (Terminalia Chebula) - The Herbal Medicine

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ABSTRACT:-Terminalia Chebula (Harde) is reported to possess Bioactive compounds like Tannins-[Chebulic acid, Chebulinic acid, Chebulagic acid, Gallic acid, Corilagin, Elagic acid], Flavonoids,sterols, Aminoacids, Fructose, Resin & Fixed oils which are confirmed to have different diverse pharmacological activities. Terminalia Chebula plant is reported to have diverse Pharmacological activities like Antioxidant Activity, Anti-HSV-2 Activity, Anti-Bacterial Activity, Anti-cancer Activity, Anti-Cryptococcal Activity, Anti-Convulsant Activity, Immunomodulatory Activity, Analagesic Activity, Anti-Inflammatory Activity, Anti-Hyperlipidemic Activity, Anti-Ulcer Activity, Anti-Diabetic Activity & Anti-Fungal Activity. Terminalia Chebulla is used in the treatments of various ailments. The diverse ailments like Cancer, Inflammation, Diabetes, Hyperlipidemia and other infectious diseases.

KEYWORDS:- Harde, Haritaki, Terminalia Chebula , Pharmacological activity, Myrobalane

I. INTRODUCTION:-

Terminalia chebula (T. chebula) is a branched deciduous tree. The fruits of the plant are reported to be used as an astringent, laxative, stomachic, tonic, anthelmintic and to cure gum bleeds.[1] Its nut-like fruits are reputed to have many therapeutic uses including antibacterial, purgative, as an astringent, and as a blood purifier in Ayurvedic and Thai folk medicines.[2] Terminalia chebula Retzius is an ethnopharmacological plant of India and Southeast Asia, and has traditionally been used as a laxative, a diuretic, and an anti-oxidative material.[3] Terminalia chebula Retz. is called the "king of medicines" in Tibet and is always listed first in the Ayurvedic meteria medica because of its extraordinary powers of healing.[4] T. chebula is a popular traditional medicine in India and East Asia. It exhibits a variety of in vivo pharmacological activities, such as anti-aging, anti-ulcer, cardioprotection, and wound healing.[5] T.chebula is used to treat urolithiasis and is actively used in various drug formulations of kidney stone treatments like neeri.[6] T. chebula Retz medium sized up to 25m tall, deciduous tree of variable appearance with usually short cylindrical bole of 5-10m length, 60-80cm in diameter.[7] T. chebula have a number of pharmacological activities due to the presence of various types of bioactive compounds, particularly on inflammatory conditions like arthritis and gout, the possible mechanism of anti-inflammatory action could be due to inhibition of inducible nitric oxide synthase.[8]

INTRODUCTORY PROFILE:-[9]

Biological source:- Flowering evergreen tree attaining a height up to 30m, with widely spread branches and a brown rounded crow.
Family:- Combretaceae

TAXONOMICAL PROFILE:-[10]

Kingdom: Plantae-Plants
Subkingdom: Tracheobionta-Vascular plants
Superdivision: Spermatophyta-seed plants
Division: Magnoliophyta-flowering plants
Class: Magnoliopsida-dicotyledons
Subclass: Rosidae
Order: Myrtales
Family: Combretaceae-Indian almond family
Genus: Terminalia L-tropical almond
Species: T. chebula (Geartn) Retz.-myrobalan.

SYNONYMES[11]:-

India: Haritaki, Harad, Hirada, Alalekayi, Kadukkai, Horitoky, Hilikha, Karakkaya
Srilanka: Aralu
China: Zhang-Qin-Ge, Hezi
Tibet: Harra, Harro
Germany: Myrobalane
France: Myrobalan

CHEMICAL CONSTITUENTS:-[12]

T. chebula contains:-

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- Tannins
- Flavonoids
- Sterols
- Aminoacids
- Fructose
- Resin
- Fixed oils.

Main components of tannins are:-

- Chebullic acid
- Chebulinic acid
- Chebulagic acid
- Galic acid
- Corilagin
- Ellagic acid.

II. MACROSCPICAL CHARACTERISTICS[11],[13]:-

It is a deciduous tree, younger stems glabrescent, woody. Leaves are 10-20 cm long, sub-opposite, simple, exstipulate, petiolate, at the base of the lamina on the petiole two prominent gland were present, lamina broadly elliptic to elliptic – oblong, rarely ovate, the bases obtuse, the margins entire, the tips acute, glabrescent.

Sr.No.	Macroscopic Characters	Fruits of Terminalia chebulla
1.	Colour,Odour and Taste	Yellowish brown to blackish brown in colour externally and darker with dirty white patches internally; Characteristic odour & astringent in taste
2.	Surface	Longitudinally wrinkled and shiny
3.	Size and Shape	Round to ovoid, upto 4 cm in length and 2.5 cm wide; pericarp excluding endocarp upto 4 mm in thickness
4.	Texture and Fracture	Hard and rough, fracture granular

Figure: Fruits

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Figure: Pericarp excluding endocarp

III. MICROSCOPICAL CHARACTRISTICS[13]:-

Transverse section of pericarp (excluding endocarp) shows, epicarp consisting of tangentially elongated single layer of epidermal cells covered with cuticle and embedded with brownish content, followed by mesocarp consists of 2-3 layers of collenchymatous hypodermis, followed by wide zone of thin walled parenchymatous cells embedded with tannin content, starch grains, rosette and cluster crystals of calcium oxalate; sclereids, stone cells and vascular bundles of various size and shape are arranged in horizontally elongated in the peripheral region and radially running ones in the interior portion.

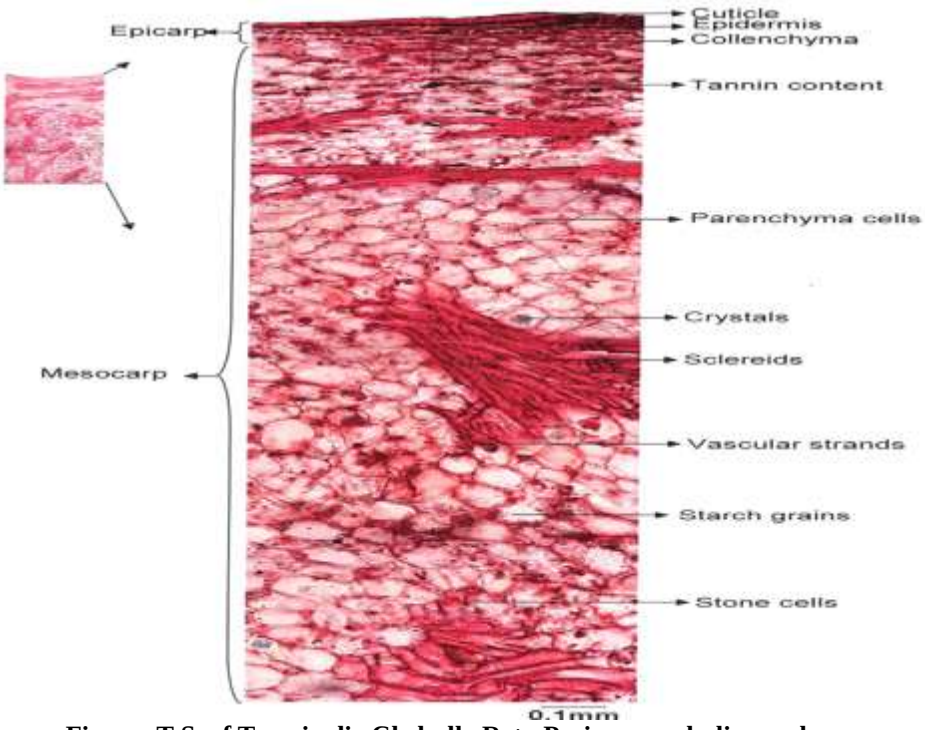

Figure: T.S. of Terminalia Chebulla Retz-Pericarp excluding endocarp

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IV. DIFFERENT PHARMACOLOGICAL ACTIVITY:-

[1] Antioxidant Activity[14]:-

In the present study, the antioxidant role of Terminalia chebula aqueous extract was evaluated against age-related oxidative stress in heart tissues of young and aged rats. Young and aged rats were treated with T. chebula aqueous extract at a dose of 200mg/kg body weight in 1.5ml sterile water orally for 4 weeks. Control young and aged rats were received sterile water only. In aged rats, the increased content of malondialdehyde (MDA) was observed. The antioxidants, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activities, reduced glutathione (GSH), vitamin C and E levels were decreased in heart tissues of aged control rats. Administration of T. chebula to aged rats prevented the depletion of SOD, CAT, GPx activities and GSH, vitamin C and E contents. Also, the level of MDA content was decreased in heart tissues. The results of the present study show that T. chebula aqueous extract modulates the activities of antioxidants and lipid peroxidation through the management of oxidant/antioxidant imbalance in rat heart tissues.

[2] Anti-HSV-2 Activity[15]:-

Development of new and effective therapeutics for sexually transmitted herpes simplex virus-2 (HSV-2) infection is important from public health perspective. With an aim to identify natural products from medicinal plants, in the present study, the potential of Terminalia chebula Retz was investigated for its activity against HSV-2. Fruits of Terminalia chebula Retz were used to prepare 50% ethanolic extract. In addition, chebulagic acid and chebulinic acid both purified from T. chebula were also used. The extract as well as purified compounds were first used to determine their in vitro cytotoxicity on Vero cells by MTT assay. T. chebula extract, chebulagic acid, chebulinic acid along with acyclovir were subsequently assessed for direct anti-viral activity, and their ability to inhibit attachment and penetration of HSV-2 to the Vero cells. In addition, their anti-HSV-2 activity was also determined by in vitro post-infection plaque reduction assay. Cytotoxicity assay using Vero cells revealed CC50 = 409.71 ± 47.70 µg/ml for the extract whereas chebulagic acid and chebulinic acid showed more than 95% cell viability up to 200 µg/ml. The extract from T. chebula (IC50 = 0.01 ± 0.0002 µg/ml), chebulagic (IC50 = 1.41 ± 0.51 µg/ml) and chebulinic acids (IC50 = 0.06 ± 0.002 µg/ml) showed dose dependent potent in vitro direct anti-viral activity against HSV-2.

[3] In Vitro Anti-Bacterial Activity[16]:-

The leaf galls of Terminalia chebula is used widely as Karkatasringi in south Indian markets. Karkatashringi is an important crude drug employed in various indigenous systems of medicine against several diseases and the drug has diverse medicinal properties. The present study was carried out to understand the antimicrobial activity of various extracts. The antibacterial activity of T. chebula (leaf gall) was evaluated against ten bacterial strains including Gram-positive and Gram-negative bacteria using the agar-well diffusion method. Among the two extracts tested, the ethanol extract presented the best results against all the bacteria while aqueous extract showed moderate inhibition of the microbial growth. Each extract is unique against different microorganisms; Staphylococcus aureus was more susceptible to both extract among the tested organisms, whereas Serratia marcescens and Proteus mirabilis were less susceptible for ethanol and aqueous extract respectively. The inhibitory effect of the extracts was compared with standard antibiotic Ciprofloxacin.

[4] Anti-Bacterial Activity[17]:-

The preset study was framed out to evaluate the phytochemicals and the antibacterial activity of the fractions separated from crude extracts of the Terminalia chebula, Momordica charantia, Dregea volubilis. Phytochemical analysis was carried out using standard such as Mayer's test, Wagner's test, Dragendorff test, Hager's Test, Alkaline copper test, Lead acetate test, Ferric chloride (FeCl3) test to identify the presence of secondary metabolites such as alkaloids, Flavonoids, Tannins in the fractions separated from the above selected plants. The test carried out for screening of phytochemicals was given positive. According to results we noticed the presence of different types of secondary metabolites such as Alkaloids, Phenols, Flavanoids, Tanins, Saponins, Carbohydrates, Amino acids in the leaf fractions. The fractions inhibited the growth of bacterial strains used in the study and exhibited antibacterial activity.

[5] Anti-Bacterial & Anti-Cancer Activity[18]:-

The present work reports a method for a facile and an eco-friendly synthesis of silver synthesis of nanoparticles (AgNPs) using

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Terminalia chebula fruit extract (TCE). The obtained AgNPs was characterized by using different spectroscopic and microscopic techniques. The analysis of the results revealed that the as-obtained AgNPs have spherical morphology with an average diameter of 22 nm. Furthermore, the preliminary bioactivity evaluations revealed that the bio-conjugation of AgNPs, using TCE, significantly enhanced the antibacterial and anti-breast cancer potentials of the latter. The antibacterial activity of the as-prepared AgNPs showed that B.subtilis was more sensitive towards the AgNPs, followed by P. aeruginosa; while, E. coli and S. mutans showed comparatively minimal sensitivity toward the AgNPs. The IC50 values of TCE, AgNPs and TCE + AgNPs treatment of MCF-7 were found to be 17.53, 14.25 and 6.484 _g/mL, respectively. Therefore, it can be ascertained that the bio-conjugation may provide a headway with regard to the therapeutic employment of T.chebula, upon mechanistically understanding the basis of observed antibacterial and anticancer activities.

[6] Anti-Cryptococcal Activity[19]:-

The increasing prevalence of multidrug resistant strains of fungi and the recent appearance of strains with reduced susceptibility to antifungal agents raises the specter of untreatable fungal infections and adds urgency to the search for new infection-fighting strategies which involves the utilization of bioactive phytochemicals from plants. The ethanolic extract obtained from the fruit of Terminalia chebula was assessed for their antifungal activity against clinical and environmental isolates of C neoformans. Extracts were prepared from the fruits by standard techniques and phytochemical analysis of the extract was performed.to study the bioactive compounds. The compounds were identified by GC MS .analysis and the functional groups were identified by FTIR. Of the 10 isolates tested the clinical isolates were more susceptible than the environmental isolates. C5and E3 was found to be more susceptible with the zone of inhibition 25mm at a concentration of 4mg/ml.. Mass spectrometric analysis revealed the presence of phenolic compounds and tannins. FTIR analysis revealed the presence of alkanes alkynes esters carboxylic acids etc. as chemical groups constituting the bioactive compounds.

[7] Immunomodulatory Activity[20]:-

To investigate the immunomodulatory activity of the alcohol extract of Terminalia chebula Retz dried ripe fruits at the cellular level. For antioxidant study, the liver mitochondria were separated and used for the estimation of enzymes catalase (CAT) and superoxide dismutase (SOD) – as well as lipid peroxidation (LPO) and reduced glutathione (GSH); Melatonin secretion was characterized using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) while spleen lymphocyte proliferation assay was performed by measuring optical density at 570 nm using ELISA reader. The cytokines, namely, IL-2, IL- 10 and TNF-_ expression in spleen cells, were determined by real time polymerase chain reaction (RTPCR). Terminalia chebula extract (100 mg/kg/p.o.) increased the level of liver mitochondrial enzymes CAT and SO) as well as GSH but decreased the level of LPO in the liver when compared to the vehicle, sheep red blood cells (SRBC) and cyclophosphamide-treated groups. Secretion of melatonin by pineal gland was enhanced by T. chebula treatment. The extract also increased spleen lymphocyte proliferation. Based on RT-PCR analysis, the expression of cytokines, viz, IL-2, IL-10 and TNF-α, was more in T. chebula-treated than in vehicle- and cyclophosphamide- treated groups.

[8] Anti-Convulsant Activity[21]:-

The aim of the present study was, therefore, to evaluate the anticonvulsant potential of the ethanol extract of fruits of Terminalia chebula (EETC) in experimental animal models, to provide a pharmacological justification for the traditional use of the plants fruits in the management of epilepsy in some rural parts of India. The anticonvulsant activity of ethanolic extract of fruits of Terminalia chebula (200 and 500 mg/kg, p.o.) in mice was assessed by using maximum electroshock seizure (MES) test, Pentylenetetrazole (PTZ), and picrotoxin (PC) test. The ethanolic extract of Terminalia chebula significantly reduced the duration of seizures induced by maximal electroshock (MES). The ethanol extract in doses of 200 and 500 mg/kg conferred protection (17 and 50%, respectively) on the mice. The same doses also protected animals from pentylenetetrazole-induced tonic seizures and significantly delayed the onset of tonic seizures produced by picrotoxin.

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[9] Analgesic & Anti-Inflammatory Activity[22]:-

The present study was undertaken to evaluate the analgesic and anti-inflammatory activities of ethanolic extract of Terminalia chebula (commonly known as Haritaki) fruits in experimental animal models. The study was carried out using Swiss Albino mice (20 - 25 g) and Long Evans rats (100 - 150 g) of either sex. The analgesic activity of Terminalia chebula was assessed by using hot plate method. For the determination of analgesic effect, doses of ethanolic extract of Terminalia chebula used in the present study were 250 mg/kg and 500 mg/kg body weight (BW). Anti-inflammatory effect was analyzed by carrageenan induced paw edema method with the administration dose of 300 mg/kg BW of animals. The analysis of experimental data was performed by statistical process of ANOVA to determine the variability of sample, while Dunnet's test was performed for evaluation of comparative analgesic and anti-inflammatory activity of Terminalia chebula with control and standard. The animals were divided into four treatment groups of six animals each and the "Mean ± SEM" is the statistical identifiable value of the data and P values <0.05 was considered statistically significant. Hot plate test showed a significant increase in the mean reaction time to heat stimuli in hot plate method at both 250 mg/kg and 500 mg/kg BW doses throughout the observation period in 30 minutes and 60 minutes after treatment, which was comparable to the standard ketorolac and control group. In carrageenan induced paw edema method, considerable results were found after determining the percentage change in paw volume in extract. In both cases of analgesic and an-ti-inflammatory study, % inhibition of pain and inflammation were evaluated. Comparing with control, largest inhibition was found in inhibiting inflammation 5 hours after treatment, while the largest inhibition of pain was obtained in 30 minutes and 60 minutes after treatment of doses. The present study suggests that ethanolic extract of Terminalia chebula fruits has significant analgesic and anti-inflammatory activities.

[10]Anti-Hyperlipidemic Activity[23]:-

Hyperlipidemia is known to be a major risk factor for the development of cardiovascular diseases (CVDs) which include atherosclerosis, coronary heart disease, and stroke. Although there are a large number of anti-hyperlipidemic drugs available, unfortunately, they all have side effect. Terminalia chebula Retz. (Combretaceae) is a plant used to treat cardiac disorders in the traditional Ayurveda medicine in India. The objective of this study was to assess the anti-hyperlipidemic properties of a methanol (MeOH) bark extract of T. chebula. Acute toxicity studies were performed according to the Organisation for Economic Cooperation and Development (OECD) guideline no. 423 using various doses (5, 50, 300, and 2000 mg/kg) of T. chebula bark. Anti-hyperlipidemic effect of MeOH bark extract of T. chebula at doses of 200, 400, and 600 mg/kg and fasting glucose levels after treatment with MeOH bark extract of T. chebula at doses of 200, 400, and 600 mg/kg were analyzed using commercially available kits. Acute toxicity studies did not show any morbidity and mortality at various doses. The MeOH extract of T. chebula bark at doses of 200, 400, and 600 mg/kg significantly lowered serum cholesterol and triglyceride levels. Moreover, the extract of T. chebula and the positive control atorvastatin-treated groups of animals showed a significant increase in the serum highdensity lipoprotein (HDL) cholesterol levels in diet-induced hypercholesterolemic animals.

[11]Anti-Ulcer Activity[24]:-

Terminalia chebula Retz. (Combretaceae) is a medium-sized tree that grows in the wild throughout India. T. chebula has been extensively used in Ayurveda, Unani, and homoeopathic medicine. The fruit has been used as a traditional medicine for a household remedy against various human ailments. Traditionally T. chebula is used to cure chronic ulcer, gastritis, and stomach cancers. The present study is to evaluate the antiulcer effect of hydroalcoholic (70%) extract of Terminalia chebula fruit. Aspirin, ethanol and cold restraint stress-induced ulcer methods in rats were used for the study. The effects of the extract on gastric secretions, pH, total and free acidity using pylorus ligated methods were also evaluated. Animals pretreated with doses of 200 and 500 mg/kg hydroalcoholic extract showed significant reduction in lesion index, total affected area and percentage of lesion in comparison with control group ($P < 0.05$ and $P < 0.01$) in the aspirin, ethanol and cold restraint stress-induced ulcer models. Similarly extracts increased mucus production in aspirin and ethanol-induced ulcer models. At doses of 200 and 500 mg/kg of T. chebula extract showed antisecretory activity in pylorus ligated model, which lead to a reduction in the gastric juice volume, free acidity, total acidity, and significantly increased gastric pH.

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[12]Anti-Diabetic Activity[25]:-

The present study was aimed to evaluate the Anti-Diabetic potential of Terminalia chebula fruits on streptozotocin (STZ)-induced experimental diabetes in rats. Oral administration of ethanolic extract of the fruits (200 mg/kg body weight/rat/day) for 30 days significantly reduced the levels of blood glucose and glycosylated hemoglobin in diabetic rats. Determination of plasma insulin levels revealed the insulin stimulating action of the fruit extract. Also, the alterations observed in the activities of carbohydrate and glycogen metabolising enzymes were reverted back to near normal after 30 days of treatment with the extract. Electron microscopic studies showed significant morphological changes in the mitochondria and endoplasmic reticulum of pancreatic β cells of STZ-induced diabetic rats. Also, a decrease in the no. of secretory granules of β-cells was observed in the STZ-induced diabetic rats and a these pathological abnormalities were normalized after treatment with T.chebula extract. The efficacy of the fruit extract was comparable with glibenclamide, a well known hypoglycemic drug.

[13] Anti-Fungal Activity[26]:-

The present study was aimed to investigate the anticandidal and antifungal potential of dried fruit extracts of Terminalia chebula against Candida albicans, C. tropicalis C. glabrata, C. krusei, C. parapsilosis, and Aspergillus flavus, A. niger, A. fumigatus, Trichophyton mentagrophytes, T. rubrum, Microsporum gypseum. Phytochemical analysis of methanol extracts of T. chebula dried fruits showed the presence of flavonoids, alkaloids, glycosides, saponins, tannins, terpenoids and steroids. Among the tested four extracts, the methanol extracts of T. chebula dried fruits exhibited the highest antifungal activity and their inhibition zone was ranged between 7.5 to 19.5mm. MIC and MFC values were between 62.5-250µg/ml and 250-500µg/ml respectively. Zone of inhibition (19.5 mm), MIC (62.5µg/ml) and MFC (125µg/ml) values observed in methanolic extracts of T. chebula dried fruits against A. fumigates and T. mentagrophytes. The antifungal activity of ethyl acetate, hexane, chloroform and methanol crude extracts of T. chebula dried fruits was possessed different degrees of activity against five Candidal strains, three Aspergillus species and three dermatophytic fungal strains.

V. CONCLUSION:-

Conclude that Harde prevents innumerable health diseases and disorders. It's extracts and herbal formulation decipited potential for therapeutic benefits on a similar line shown by standard drugs against various diseases.

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